REMARKS

The Examiner has rejected claims 1-33 as indefinite under 35 U.S.C. §112. In particular, the Examiner states that claims 1 and 22 (which Applicant assumes is in fact claim 21) are indefinite due to an improper Markush group. The Examiner suggests that the Markush groups of claims 1 and 21 should properly be concluded with "and *Arachnia propionica*." The Examiner further states that the species listed are not *P. acnes*, but are different species of bacteria. In addition, the Examiner indicates that the phrase "but not limited to" in several claims is unclear and therefore indefinite. Accordingly, Applicant has amended claims 1, 8, 9, 21, 24, and 25 as suggested by the Examiner, to more particularly point out and distinctly claim the subject matter of the invention. Applicant respectfully submits that the claims are now definite.

The Examiner further rejects claims 1-33 under 35 U.S.C. §103(a) as obvious in light of Adlam et al., Evans et al., Fujiwara et al., Howard et al., Megid et al., and Neifeld et al. Specifically, the Examiner contends that Adlam, Evans, Fujiwara, Howard, Megid, and Neifeld all teach the administration of *C. parvum* or *P. acnes* to a patient to cause an antineoplastic and/or antiviral effect. The Examiner further states that what is not taught is the specific use of the bacteria for the tumor claimed in claim 1 or the specific use of the bacteria to treat viral lung infections in humans. However, the Examiner relies on the alleged breadth of the prior art to state that it would have been obvious at the time the invention was made to treat dermal tumors and viral lung infections by administering the bacteria to a patient in need thereof.

Briefly, the prior art documents presented by the Examiner teach the following. Adlam teaches to provide an intravenous injection of killed *P. acnes*, that is killed by the addition of formalin. Evans teaches to provide non-specific immunotherapy to horses to treat chronic respiratory disease by means of an intravenous injection of an ethanol suspension of inactivated

P. acnes. Fujiwara teaches the injection of *P. acnes* to reduce metastasis formation in mice, although the growth of the primary tumor is not effected. Howard teaches the pre-treatment of a mouse with a standard suspension of killed *C. parvum* to develop an adjuvant effect in the mouse to cause a B-cell response to T-independent antigen SIII. Megid demonstrates antiviral activity by systemic treatment of mice infected with a rabies virus using *P. acnes* as an immuno-modulator, which is a non-specific stimulator of the immune system that may affect humoral and cellular functions of immunity. Megid, however, did not reveal encouraging results. Neifeld teaches that intratumoral immunotherapy using intralesional injection and subcutaneous application of *C. parvum* is ineffective. Specifically, Neifeld provides that injecting *C. parvum* into tumors or administering same subcutaneously does not have a beneficial effect on primary cancers of the oral cavity, pharynx, and larynx.

Applicant respectfully traverses the Examiner's rejection. To present a prima facie case of obviousness the Examiner must show: 1) that there is some suggestion in the art or the references themselves to combine or modify the references to show the invention was obvious; 2) that there is a reasonable expectation of success; and 3) that the prior art reference or references teach or suggest all the claim limitations. MPEP 2142. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990); MPEP 2143.01. In the present case, the Examiner combines the prior art teaching that the administration of *C. parvum* and *P. acnes* causes an antineoplastic or antiviral effect with the alleged breadth of prior art showing non-specific immunological benefits when the bacteria is administered to humans or other animals, and the alleged large number of animal

studies that correlate well to human usage, to show it would have been obvious to treat dermal tumors and viral lung infections by administering bacteria to a patient in need thereof.

Claims 1 and 21 have been amended to further define that the bacteria that is administered is heat-killed, terminally sterilized bacteria. The specification provides antecedent support for terminal sterilization of the heat-killed bacteria. *Specification, pg. 7, lines 18-19.* Claim 21 has been further amended to provide that infections of the respiratory tract in humans are treated by administering the heat-killed, terminally sterilized bacterial product of the present invention. As the disclosure of the invention indicates, the treatment of infections of the respiratory tract of the present invention is not limited to viral infections, but other infections of the respiratory tract in humans, such as bacterial infections, can also be effectively treated by the administration of the bacteria of the present invention. *Specification, pg. 8, lines 18-19; pg. 9, lines 14-16; pg. 10, lines 12-14.* Claims 34 – 36 have been added to describe the specific administration of the bacterial product to generate the desired result. Specifically, Claim 34 has been added to provide that the regression of dermal tumors in humans may be obtained through intralesional administration of heat-killed, terminally sterilized bacteria. Claim 35 has been added to provide that the regression of dermal tumors in humans may also be obtained through subcutaneous administration of heat-killed, terminally sterilized bacteria. Claim 36 has been added to provide that heat-killed, terminally sterilized bacteria is orally administered to treat infections of the respiratory tract in humans. Claims 16, 17, and 30 provide antecedent support for the intralesional, subcutaneous, and oral administration of the bacteria, respectively. Care has been taken to avoid the addition of new matter to the claims.

Turning to the Examiner's rejections, Applicant respectfully requests that the Examiner provide references, for Applicant's review, in support of the Examiner's assertions of the general

teachings in the art regarding non-specific immunological benefits that occur when bacteria are administered to humans or other animals, and the particular animal studies that correlate well to human usage to which the Examiner refers.

Secondly, the Examiner is asserting that it would have been obvious to treat dermal tumors and infections by the specific method claimed in claims 1 and 21 by combining the cited references, which teach, generally, the administration of *C. parvum* or *P. acnes* to a patient to cause an antineoplastic and/or antiviral effect, with the alleged breadth of prior art that exists showing non-specific immunological benefits that the art recognizes for humans or animals, and the alleged large number of animal studies that correlate well to human usage. In other words, the Examiner is claiming that based on the non-specific prior art, and a correlation between animal and human usage, it would have been "obvious to try" the specific administration *P. acnes* of the claimed invention. By indicating that it would have been obvious to try the claimed invention, the Examiner is impermissibly relying on hindsight to show the Applicant's claimed invention is obvious.

The Federal Circuit has held that a similar situation presented an impermissible "obvious to try" rejection by an examiner. In *Amgen Inc. v. Chugai Pharmaceutical Co.*, the defendants attempted to show that an invention claiming the use of an EPO gene as a probe in humans was obvious in light of an already known use of a monkey EPO gene as a probe. *Amgen Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). The evidence indicated that monkey and human DNA were roughly 90 percent homologous. *Id.* Therefore, it was claimed that it would have been obvious to probe a human DNA library with a monkey DNA probe. *Id.* The court indicated that this homology may have indicated that it would be obvious

to try the claimed invention, but the homology alone was not sufficient to conclude that the claimed invention could have been carried out with a reasonable likelihood of success. *Id.*

In the present case, the Examiner claims that a large number of animal studies correlate well to human usage. If such a large correlation in fact exists, the correlation on its own is not sufficient to show the claimed invention could be carried out with a reasonable likelihood of success, as indicated by the court in *Amgen*. *See id.* Accordingly, the alleged correlation between animals and humans cited by the Examiner, at most, indicates it would have been obvious to try the claimed invention. Moreover, the prior art demonstrates non-specific administration of *P. acnes* to produce an antiviral or anti-tumor effect. The prior art does not demonstrate, nor suggest, the administration of *P. acnes* to induce the regression of dermal tumors in humans or to treat infections of the respiratory tract in humans. Furthermore, the prior art does not teach to administer heat-killed, terminally sterilized bacteria to accomplish the above results. Accordingly, combining the cited prior art with the correlation between animals and humans does not present a reasonable likelihood that the specific administration of *P. acnes* of the claimed invention would be successful.

In addition to a reasonable likelihood of success, there must be a suggestion in the prior art to combine the prior art references to show the invention is obvious. In the present case, no suggestion to combine the cited references exists. The prior art teaches the general administration of the bacteria through, for example, intravenous, intraperitoneal or intrathoracic methods. It does not teach, nor suggest, the administration of the bacteria which is directed to a dermal tumor in humans to cause the regression of same, or the administration of bacteria which is directed to the treatment of infections of the respiratory tract in humans. Further, the prior art

does not teach the specific intralesional, subcutaneous, or oral administration of the bacteria to accomplish the above-mentioned results.

The intravenous injection of *P. acnes* or *C. parvum,* as taught by Adlam, Evans, and Megid is a non-specific administration of the bacteria that generates a general immune response. Fujiwara teaches the injection of *P. acnes* to reduce metastasis formation. Similarly, Howard provides for the pre-treatment of an animal to generate an adjuvant effect. Both of these treatments are non-specific to the target area intended to be affected. Additionally, Neifeld, while showing the injection *C. parvum* intralesionally and subcutaneously, provides that such treatment is ineffective and does not have a beneficial effect, thus teaching away from the present invention. Likewise, Megid did not reveal encouraging results, and therefore, also teaches away from the claimed invention.

In addition, Adlam teaches to kill *P. acnes* by the addition of formalin, while Evans teaches to add ethanol to *P. acnes*, both of which are painful to, or cause reactions in humans if not administered appropriately. This is contrary to the claimed invention, the purpose of which is to provide a means of safely and adequately inactivating the *P. acnes* and reducing the pain associated with many conventional treatments. *Specification, pg. 4, lines 15-27.* This purpose is accomplished in the present invention by using heat-killed, terminally sterilized bacteria. *Specification, pg. 5, line 24-pg. 6, line 2.* The use of heat-killed, terminally sterilized bacteria does not require the use of alcohol or exposure to formalin. Therefore, upon administration of same, the reaction at the site of injection is minimal. Treatment with heat-killed, terminally sterilized bacteria is more successful than the commonly used painful surgical removal of plantar warts. It is also much simpler and more successful than the use of highly toxic substances that

need to be administered multiple times to remove the warts. Furthermore, no prior art shows oral treatment of respiratory infection by use of heat-killed, terminally sterilized *P. acnes*.

Moreover, the Examiner relies on an alleged breadth of prior art teaching non-specific immunological benefits, in combination with the cited prior art references teaching the non-specific administration of *P. acnes* to show that the present invention is obvious. However, the claimed invention provides a specific administration of *P. acnes* to induce the regression of a dermal tumor in humans or to treat an infection in the respiratory tract in humans, or the specific administration by intralesional, subcutaneous, or oral means. The administration of *P. acnes* of Applicant's invention generates an immune response that is directed to dermal tumors and directed to infections of the respiratory tract. It is believed that the administration of the bacteria of the present invention, therefore, stimulates a CTL (natural killer cell) response in the targeted area. Additionally, in the case of infections of the respiratory tract in humans, the administration of the bacteria of the present invention is also believed to stimulate phagocytosis at the targeted site, aiding in the treatment of the targeted area. Furthermore, none of the cited references teach or suggest the administration of heat-killed, terminally sterilized bacteria to induce the regression of dermal tumors in humans or to treat infections of the respiratory tract in humans. As the prior art only teaches the general administration of *P. acnes* to generate a general immune response, it does not teach or suggest the administration of heat-killed, terminally sterilized bacteria that directs an immune response to induce the regression of dermal tumors in humans, or to treat infections of the respiratory tract in humans.

Additionally, the Examiner has not demonstrated that all the elements of the claimed invention are disclosed in the combination of references. As discussed herein, the Examiner relies on prior art showing the non-specific administration of bacteria to attempt to demonstrate

the specific administration of bacteria of Applicant's claimed invention. The Examiner has not shown the administration of the bacteria to induce the regression of dermal tumors in humans, or the treatment of infections of the respiratory tract in humans. Likewise, the Examiner has not demonstrated the administration of heat-killed, terminally sterilized bacteria to induce the regression of dermal tumors in humans, or the oral administration of same to treat infections in the respiratory tract in humans. Accordingly, the Examiner has not demonstrated that all the elements of the claimed invention are taught by the prior art.

Moreover, Applicant notes that the general technology of using *P. acnes* for its antiviral and antineoplastic activity has been available for many years. Yet, despite this use and a long-felt need, it has not been shown to administer heat-killed, terminally sterilized bacteria to induce the regression of dermal tumors in humans, or to treat infections of the respiratory tract in humans.

Furthermore, contrary to the Examiner's contention, the various proportions and amounts of ingredients used in the claimed invention could not be obtained without undue experimentation. Accordingly, these proportions and amounts are not result effective variables, and therefore are not obvious in light of the references disclosed. Moreover, as discussed herein, the invention as claimed in independent claims 1, 21, and 34-36 is not obvious in view of the cited references. Therefore, the proportions and amounts of ingredients listed in the associated dependent claims are not obvious in light of same.

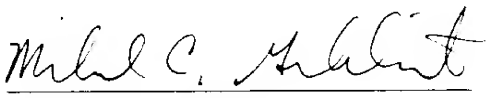
Accordingly, the prior art does not teach or suggest the administration of heat-killed, terminally sterilized bacteria into a dermal tumor in humans or the administration of bacteria to treat infections of the respiratory tract in humans. Likewise, the prior art does not teach the

specific intralesional, subcutaneous, or oral means of administration of the bacteria. Thus, Applicant respectfully submits that the pending claims are allowable over the prior art.

CONCLUSION

In light of the foregoing Amendments and Remarks, Applicant respectfully submits that claims 1-36 are now in condition for allowance.

Respectfully submitted.



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Marked-Up Claims

1. (amended) A method of inducing the regression of dermal tumors in humans which comprises the step of administering a bacterial product comprising heat-killed, terminally sterilized [*P. acnes*] bacteria selected from the group consisting of *Propionibacterium acnes*, *Propionibacterium avidum*, *Propionibacterium lymphophilum*, *Propionibacterium granulosum*, *Cornynebacterium parvum*, and [or] *Arachnia propionica*.

8. (amended) The method of claim 7, wherein the carriers comprise [are] sugars selected from the group consisting of [sugars including but not limited to] lactose, saccharose, mannitol, sorbitol, and cellulose preparations.

9. (amended) The method of claim 7, wherein the carriers comprise [are selected from the group consisting of] amino acids [including but not limited to glycine].

21. (amended) A method of treating [viral] infections of the respiratory tract in humans which comprises the step of administering a bacterial product comprising heat-killed, terminally sterilized [*P. acnes*] bacteria selected from the group consisting of *Propionibacterium acnes*, *Propionibacterium avidum*, *Propionibacterium lymphophilum*, *Propionibacterium granulosum*, *Cornynebacterium parvum*, and [or] *Arachnia propionica*.

24. (amended) The method of claim 23, wherein the carriers comprise [are] sugars selected from the group consisting of [sugars including but not limited to] lactose, saccharose, mannitol, sorbitol, and cellulose preparations.

25. (amended) The method of claim 23, wherein the carriers comprise [are selected from the group consisting of] amino acids [including but not limited to glycine].